REMARKS

Claims 31-44 are pending in this application. Claims 1-30 have been canceled without prejudice or disclaimer and new claims 31-44 have been added herewith.

In the specification amendments, the term "rectum" has been changed to –colon– in Table 1 and on page 27. Applicants assert that no new matter is added by this amendment, as this represents a translation error in the original specification. It is apparent that the original "rectum cancer" was an error, since this was apparently redundant with the listing of "rectal cancer". This amendment has also been reflected in new claim 39.

Regarding Election/Restriction.

Applicants assert that new claims 31-44 read on the elected Group I and species as indicated in the Response of August 23, 2001.

Regarding claim for foreign priority.

A claim for foreign priority and the certified copy of the priority document are being filed concurrently with this Amendment. A verified translation of the priority document is attached to this Amendment.

The specification is objected to.

The Examiner objects to the specification for not containing a reference to the priority status in the first line of the specification.

Applicants respectfully traverse this objection. Applicants note that the present application claims foreign priority under 35 U.S.C. 119 of a Japanese patent application. The Examiner appears to be referring to the requirement under 37 C.F.R 1.78(a)(2), for reference in the application to prior copending nonprovisional applications or international (PCT) applications. However, this requirement does not extend to the claim for priority of a foreign patent application, as in the present case. The claim for foreign priority in the present application was originally made in the Declaration and the certified copy of the priority document has now been filed. Applicants respectfully assert that it is unnecessary to amend the present specification as suggested by the Examiner.

Claims 4 and 16 are objected to.

The objection is overcome by the cancellation of claims 4 and 16 without prejudice or disclaimer.

Claims 2 and 12-13 are objected to.

The objection is overcome by the cancellation of claims 2, 12 and 13 without prejudice or disclaimer.

Claims 1-4, 6-7, 11-13, 16 and 18-19 are rejected under 35 U.S.C. 112, second paragraph, as indefinite.

The rejection is overcome by the cancellation of claims 1-4, 6-7, 11-13, 16 and 18-19 without prejudice or disclaimer. Applicants assert that new claims 31-44 are definite with regard to the issues raised by the Examiner.

Claims 11-13, 16 and 18-19 are rejected under 35 U.S.C. 112, second paragraph, as indefinite.

The rejection is overcome by the cancellation of claims 11-13, 16 and 18-19 without prejudice or disclaimer. Applicants assert that new claims 31-44 are definite with regard to the issues raised by the Examiner. The new claims do not include the phrase "using".

Claims 1-3 and 11-13 are rejected under 35 U.S.C. 102(b) as anticipated by Nagata et al. (*Tumor Biol.* 1991).

Claims 1-3 and 11-13 have been canceled without prejudice or disclaimer. Applicants here address this rejection with regard to new claims 31-44.

New independent claim 31 recites a specific method involving three main steps. Step (i)(a) of the method involves the mixing of a first protein that selectively binds a particular (first) sugar chain structure with a first portion of a sample containing CEAs, to form a complex between the protein and those CEAs containing the particular sugar chain structure. Step (ii)(a) involves adding a second protein to a second portion, the second protein binding to a different (second) sugar chain structure. Step (iii) involves determining the presence of a particular cancer based on whether complexes are detected in steps (i)(b) and (ii)(b).

New claim 31 differs from Nagata et al. in several respects.

First of all, Nagata et al. discloses a sandwich assay for carcinoembryonic antigen. In the assay, lectin agarose beads were used to bind certain CEAs, and these were further reacted with ^{125}I-labeled anti-CEA monoclonal antibody (MoAb). The ^{125}I-label associated with the beads was then

counted. Seven different lectins were studied: wheat germ agglutinin, *P. vulgaris* erythroagglutinin and leukoagglutinin, *R. Communis* agglutinin-1, peanut agglutinin, concanavilin-A, and *Lens culinaris* agglutinin (page 36, column 1).

Therefore, Nagata et al. uses lectins, while claim 31 recites use of a first protein and a second protien to bind sugar chain structures.

Secondly, Nagata et al. indicates that the described L-IRMA technique may allow for **investigating** the heterogeneity of sugar chains on the CEA molecule by using lectins specific for specific sugar chains (page 43, 1st column).

However, Nagata et al. does not disclose making a determination as to whether cancer is present based on results obtained using two different lectins on a single sample. Nagata does indicate that some individual lectin binding may be used as markers, for example, CEA in metastatic hepatoma (page 43, 1st column), but does not appear to indicate that results from two or more lectins, in particular three as in claim 32 or four as in claim 33, might be particularly indicative. Nagata's indication that the technique may allow for "investigating the heterogeneity of sugar chains" provides only an invitation to study correlations between lectin binding and cancer.

Nagata et al. also clearly does not suggest the specific recitations of claims 34-44.

Claims 1-4, 6 and 7 are rejected under 35 U.S.C. 102(b) as anticipated by Mach et al. (*Annals of the NY Acad. Sci.* 1975, vol. 259, pages 389-403).

Claims 1-4, 6 and 7 have been canceled without prejudice or disclaimer. Applicants here address this rejection with regard to new claims 31-44.

With regard to claim 31, Mach et al. does not disclose separate assays using two proteins on

two portions of the same sample as recited in the claim.

Mach et al. discusses immunoassays for CEA. The Examiner refers in particular to figure 4 on page 394 of the reference. Figure 4 discloses a gel precipitin assay of CEA and glycoprotein with blood group activity. Specifically, this assay involves use of an anti-CEA antibody and an anti-Lewis+ or anti-blood group A antibody, along with CEA. This assay shows the correlation between the anti-CEA and anti-Lewis+ or anti-A activity. The assay does **not** appear to be based on simultaneous binding of the anti-CEA antibody and the anti-Lewis+ or anti-A antibody to a single CEA molecule.

The Examiner also refers to Fig. 7, which shows the elution patter of radiolabeled CEA on sepharose when bound by anti-CEA antiserum or anti-B antiserum. Applicants note that this assay does not appear to involve simultaneous addition of anti-CEA antiserum and anti-B antiserum to the CEA.

The Examiner also refers to Fig. 10 on page 399. Fig. 10 shows a schematic representation of an assay to detect soluble immune complexes between CEA and human immunoglobulin. In Fig. 10, on the left side, a human immunoglobulin that binds to one blood group determinant is bound to a CEA molecule having that blood group determinant. On the right side, goat IgG molecules bind to the CEA antigenic determinants. This complex can be detected by radiolabel of the CEA or by other methods.

Mach et al. also does not appear to suggest any correlation of cancer type with binding to two, three or four particular anti-blood group antibodies.

Claims 1-4, 6, 7, 11-13, 16 and 18-19 are rejected under 35 U.S.C. 103(a) as unpatentable over Mach et al. (*Annals of the NY Acad. Sci.* 1975, vol. 259, pages 389-403) in view of Pompecki et al. (*Cancer Res.* 1981) and Tannock et al. (*The Basic Science of Oncology*, 1992).

Claims 1-4, 6, 7, 11-13, 16 and 18-19 have been canceled without prejudice or disclaimer. Applicants here address this rejection with regard to new claims 31-44.

The Examiner cites Pompecki et al. (page 1907) for the selective detection of modified sugar chains on CEAs derived from cancers using lectins or antibodies. Pompecki et al. discloses a lectin and antibody-binding assay for CEA. Radiolabeled CEA was bound to lectin or antibody in the assays. Inhibition studies were performed. CEAs from five hepatic metastases of colon carcinomas were studied. The study shows that all CEA preparations bore blood group determinants. Particular activities were related to "the presence of one or both of the following unexpected oligosaccharides ...." (page 41, column 2).

However, Applicants argue that Pompecki does not disclose or suggest step (iii) in claim 31, the determination of the presence of a **particular cancer**, based on blood group determinants. Pompecki does not appear to present any data indicating that different cancer types would have different patterns of blood group determinants which would allow their discrimination. At best, Pompecki might provide an invitation to experiment in this regard. Pompecki clearly does not suggest the specific limitations of claims 38-44.

The Examiner cites Tannock as disclosing that the assay of overall CEA is already known for the detection of cancer. This reference discloses on page 201, column 1, that elevated levels of CEA are found in colorectal cancer, and that CEA is a good marker for this cancer. However, the

reference does **not** appear to discuss the nature of the sugar chain of the CEA. Therefore, Tannock does not suggest the use of two different sugar chain binding proteins as in claim 31, nor the specific recitations of the dependent claims. The correlation of total CEAs with cancer is irrelevant to the present claims.

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicants undersigned Agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

Attached hereto is a marked-up version of the changes made by the current amendment. The attached page is captioned "Version with markings to show changes made."

In the event that this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

ARMSTRONG, WESTERMAN & HATTORI, LLP

Daniel A. Geselowitz, Ph.D.
Agent for Applicants
Reg. No. 42,573

DAG/plb
Atty. Docket No. 000683
Suite 1000, 1725 K Street, N.W.
Washington, D.C. 20006
(202) 659-2930

23850
PATENT TRADEMARK OFFICE

Enclosures: Version with markings to show changes made
Verified translation of JP 11-172485

H:\FLOATERS\DAG\Amendments\000683.amend filed 8-12-02

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please replace Table 1 on page 27 with the amended Table 1:

Sample Origin	A ratio (%) of the amount of the CEAs reacted to a specific anti-sugar chain antibody (an amount of the CEAs having a specific modified sugar chain structure) relative to the amount of total CEAs			
	Anti-S-Le^a antibody	Anti-S-Le^x antibody	Anti-Le^a antibody	Anti-Le^y antibody
	%	%	%	%
Rectal cancer	1.6	___	1.1	___
~~Rectum~~ Colon cancer	___	___	___	2.0
Lung cancers	2.3	3.1	2.2 2.2	___ ___
Liver cancer	5.9	___	___	___
Oropharyngeal cancer	17.7	___	___	___
Breast cancer	___	3.3	___	5.4
Cervix uteri cancer	8.1	6.4	___	___
Matastasis of bone marrow lymph node	___	1.2	___	___
Normal human beings	___ ___ ___ ___	___ ___ ___ ___	___ ___ ___ ___	___ ___ ___ ___

Please replace the paragraph beginning on page 27, line 8 (after Table 1), with the following rewritten paragraph:

For example, in rectal cancer, S-Le^a and Le^a were detected, and in ~~rectum~~ colon cancer, Le^y; in lung cancer, S-Le^a, S-Le^x and Le^a; in liver cancer and pharyngitis cancer, S-Le^a, in breast cancer, S-Le^x and Le^y; in cervix uteri cancer, S-Le^a and S-Le^x; in matastasis of bone marrow lymph node, S-Lex were detected respectively. Namely, it is found that the kinds of the modified sugar chain structures differ among the kinds of cancers.